
Efficient siRNA delivery into primary cells by a peptide transduction domain-dsRNA binding domain fusion protein.

Journal: Nat Biotechnol

Publication Year: 2009

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PubMed link: 19448630

Funding Grants: TAT Cell-Permeable Protein Delivery of siRNAs for Epigenetic Programming of Human Pluripotent and Adult Stem Cells

Public Summary:

Scientific Abstract:

RNA interference (RNAi) induced by short interfering RNA (siRNA) allows for discovery research and large-scale screening; however, owing to their size and anionic charge, siRNAs do not readily enter cells. Current approaches do not deliver siRNAs into a high percentage of primary cells without cytotoxicity. Here we report an efficient siRNA delivery approach that uses a peptide transduction domain-double-stranded RNA-binding domain (PTD-DRBD) fusion protein. DRBDs bind to siRNAs with high avidity, masking the siRNA's negative charge and allowing PTD-mediated cellular uptake. PTD-DRBD-delivered siRNA induced rapid RNAi in a large percentage of various primary and transformed cells, including T cells, human umbilical vein endothelial cells and human embryonic stem cells. We observed no cytotoxicity, minimal off-target transcriptional changes and no induction of innate immune responses. Thus, PTD-DRBD-mediated siRNA delivery allows efficient gene silencing in difficult-to-transfect primary cell types.

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